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Johnson II T. [1], Miller M. [2], Pillion D. [3], Ouslander J. [4]
1. Atlanta VA Medical Center/ Emory University, 2. Sinai Hospital of Baltimore, Johns Hopkins Univers, 3. University of Alabama at Birmingham, 4. Emory University/Atlanta VA

ARGININE VASOPRESSIN LEVELS, RESERVE, AND ACTION IN OLDER PATIENTS WITH FREQUENT NIGHTTIME VOIDING

Aims of Study

Nocturia is common, occurring in over 50% of those over 70 years old (1). Nocturia has been associated with falling, sleep disruption, and future nursing home placement. Those with one or more episodes of nocturia per night have a 1.8 higher odds ratio of falling, and those with three or more episodes have 2.2 higher odds ratio of falling (2). Older adults rate nocturia as one of the most bothersome lower urinary tract symptoms (3, 4) and as one of the most significant causes of sleep disruption (5). Nocturnal polyuria (NP), defined as > 35% of 24 hr urine output between 11 pm and 7 am, is believed to be responsible, in part, for nocturia in many older people (6). Lack of a proper diurnal rhythm of arginine vasopressin (AVP) with increasing nighttime levels of AVP, a water-conserving hormone, has been implicated as an important cause of NP. We sought to find if other measures of AVP functioning in patients with nocturia were abnormal. Our aims were:

1. To determine what percentage of patients who averaged two or more episodes of nocturia had nocturnal polyuria (NP- defined as a production of more than 35% of total daily urine during an 8-hour period at night from 11 p.m. to 7 a.m.); and
2. For patients with NP, to determine if there were abnormalities in the secretion and/or action of arginine vasopressin as measured by AVP levels and a water deprivation test.

Methods

DESIGN: Convenience sample of adults over 65 recruited from the community
SETTING: Home setting for participant recorded voiding diaries and General Clinical Research Center (GCRC) for determination of AVP levels and water deprivation testing.
PARTICIPANTS: 44 participants who completed the 3-day clinical research stay
MEASUREMENTS: Participants recorded the time and volume of each void over a seven-day period. As they did not record the time going to bed and the time arising, we restricted our comments to "nighttime voiding" (voids during 11 p.m. to 7 a.m.) as opposed to "nocturia". Determinations of basal serum vasopressin levels were performed by radio-immunoassay from samples drawn from participants supine at night (9 p.m. – 10 p.m.) and in the morning (5 a.m. – 6 a.m.) under ad libitum fluid intake conditions. We performed water deprivation testing using a standard protocol (7). We viewed results from water deprivation testing as falling into three categories: normal; partial central AVP deficiency; and nephrogenic unresponsiveness to AVP. Normal AVP reserve and function was defined by: > or = to 500 mOsm concentration of the urine with less than a 10% increase in osmolality in response to exogenous AVP administration. Central partial deficiency of AVP was defined by a greater than 500 mOsm maximum concentration of the urine and a greater than 10% increase in osmolality in response to exogenous AVP. Nephrogenic unresponsiveness was defined as a <500 mOsm concentration in response to both water deprivation and exogenous AVP.

Results

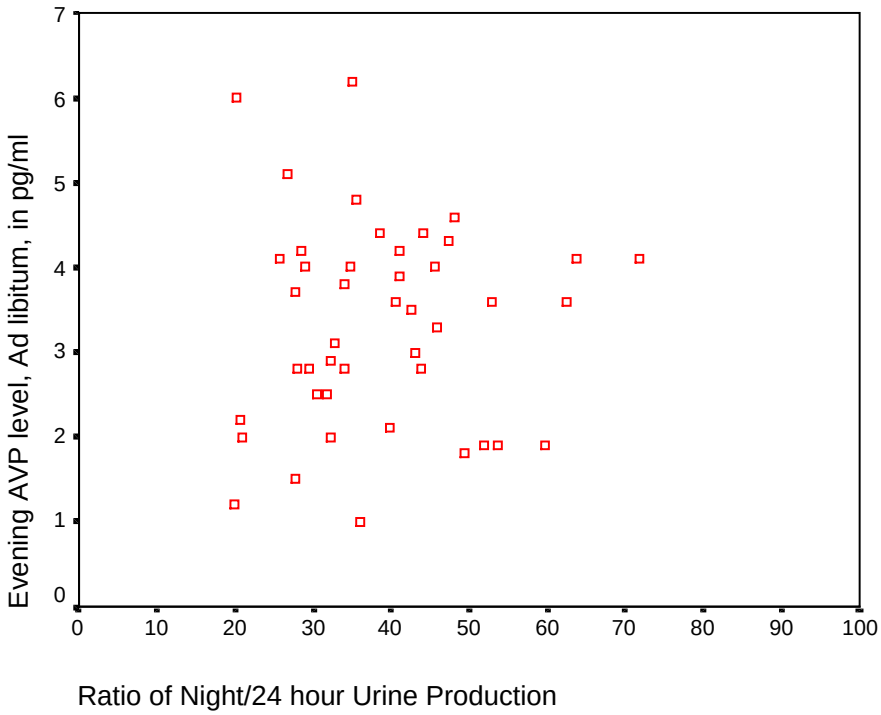
Eighty percent (36/44) of the participants averaged two or more voids per night.
There was a strong association between a higher number of nighttime voids and having a higher proportion of urine produced at night (as a proportion of the total) (correlation =0.60, $p<0.001$). Having $\geq$ 2 episodes of nighttime voiding was strongly associated with NP. Of nine persons recording <2 episodes of nighttime voiding on home diaries, only 2 had nocturnal polyuria (22 %), whereas twenty-two of thirty-five who recorded $\geq$ 2 episodes of nighttime voids had nocturnal polyuria (63%) (Chi square p=0.02).

We graphed the results of nighttime AVP serum levels versus ratio of night to total urine (**Figure 1**). The Pearson correlation for nighttime plasma AVP and night/24 hour urine ratio was 0.04 (p=0.79). Of the participants with nocturnal polyuria, eleven of twenty-five (11/25, 44%) had either central partial AVP deficiency or nephrogenic unresponsiveness to AVP. Of the participants without nocturnal polyuria, twelve out of nineteen (12/19, 63%) had either central partial AVP deficiency or nephrogenic unresponsiveness to AVP. There was no statistically significant association between AVP deficiency and having nocturnal polyuria, and in fact, the relationship trended towards showing the opposite of the expected relationship.

Conclusions

Frequent voiding at night was strongly related to nocturnal polyuria- having an abnormally high ratio of urine produced at night over the total 24-hour period. However, in this cohort of research participants, there was no direct relationship between nocturnal polyuria and AVP dysfunction as measured by serum AVP levels or water deprivation testing.

Figure 1



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Support: NIA MERIT Award (5-R37-AG08678), the GCRC at Emory University (RR00039, T5-20060), a Network 7 VA Career Development Award, and the Birmingham/Atlanta Geriatrics Research Education and Clinical Center (GRECC).